REMARKS

In an Office Action mailed January 28, 2008, the Examiner withdrew various rejections and provisional obviousness-type double patenting rejections. Withdrawal of these rejections is acknowledged.

The Examiner maintained a provisional obviousness-type double patenting rejection of claims 1, 8 and 9 over claim 48 of co-pending application 11/195,561. The Examiner maintained rejections of claims 1 and 7-11 for alleged failure to comply with the written description requirement of 35 U.S.C. § 112, first paragraph. The Examiner imposed a new rejection of claims 1-3 and 7-11, and maintained a rejection of claims 1-4, for alleged failure to comply with the enablement requirement of 35 U.S.C. § 112, first paragraph. Claims 1-5 and 11 are rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Cantello et al. (1994). Claims 1-4, 6 and 11 are rejected as allegedly anticipated by Ntambi et al. (1996). Claims 1-7 and 11 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Crooke et al. in view of Monia et al. Finally, claims 1 and 8-11 are rejected under 35 U.S.C. § 102(e) for alleged anticipation by Hayden et al.

Each ground of rejection is considered separately below. Reconsideration of the merits of this patent application is respectfully requested.

Provisional rejections for obviousness-type double patenting

Applicants stand ready to respond to these rejections upon the indication of allowable subject matter in either pending application. Response at this stage is premature.

Rejections for alleged lack of written description

The rejection is moot as applied to canceled Claim 1. The rejection of Claim 7, now presented in independent form and drawn to using an antisense oligonucleotide in a method for reducing SCD1 activity to increase insulin sensitivity, is respectfully traversed for two reasons. The level of skill in the art is such that a skilled artisan seeking an antisense oligonucleotide appropriate to reduce SCD1 activity readily understands how to select, obtain and confirm the suitability of such an oligonucleotide. The number of possible antisense oligonucleotides complementary to a portion of the polynucleotide that encodes SCD1, while high, is not unlimited or excessive. The skilled artisan can be required to undertake a significant and substantial experimentation to identify suitable oligonucleotides, but such experimentation is

permitted, as long as the required experimentation is not undue. Indeed, in accord with the state of the art, the skilled person seeking to identify appropriate oligonucleotides for use in the claimed method would routinely order candidate oligonucleotides from a commercial source. Applicants attach papers by Jiang et al. and by Gutierrez-Juarez et al. which provide post-filing confirmation of the suitability of using antisense technology to increase insulin sensitivity.

The claim is also supported by adequate written description setting forth substantial guidance to the skilled person on selection of suitable oligonucleotides. In particular, paragraph [0029] of the application as filed describes that a suitable oligonucleotide has a sequence complementary to at least part of a SCD1 mRNA sequence. The same paragraph provides an exemplary oligonucleotide having "20-25 mer antisense oligonucleotides directed against 5' end of a SCD1 mRNA with phosphorothioate derivatives on the last three base pairs on the 3' end and the 5' end to enhance the half life and stability of the oligonucleotides. A useful strategy is to design several oligonucleotides with a sequence that extends 2-5 basepairs beyond the 5' start site of transcription." Beyond this, the skilled artisan versed in the art of inhibiting translation using antisense technology is fully capable of selecting appropriate oligonucleotides for use in the method. In view of the guidance presented, Applicants need not exemplify every suitable antisense oligonucleotide.

The rejection as applied to Claims 8-11 is also traversed, as agents for accomplishing this inhibition are known to the skilled artisan. Applicants do not purport to have here invented inhibition of SCD1 enzymatic activity, but rather to have applied that knowledge to increasing insulin sensitivity, where such an increase was not appreciated prior to Applicants' development of the technology. This issue is considered further in connection with Applicants' response to the Examiner's citation of publications, below.

Rejections for alleged lack of enablement

The rejection of claims 1-3 and 7-11 is moot as applied to canceled Claims 1-3. As to the remaining claims, and as in the rejections for alleged lack of written description, Applicants maintain that the specification fully enables the skilled person to practice the invention. The skilled artisan was already familiar with ways to reduce SCD1 activity as of the filing date. Applicants extended that reduction to complete elimination by demonstrating increased insulin sensitivity in $SCD^{-/-}$ knockout animals. This observation then enabled the skilled person to

utilize SCD1-reduction tools already in his or her possession in a method for increasing insulin sensitivity.

The separate rejection of canceled Claims 1-4 for alleged lack of enablement is moot.

Rejections under 35 U.S.C. 102(b) for alleged anticipation

The rejections over Cantello (1994) of canceled Claims 1-5 are moot. The rejection over Cantello of Claim 11 is traversed as the Examiner failed to establish that any agent disclosed by Cantello inhibits SCD1 enzymatic activity by inhibiting a cytochrome b_5 protein, a NADH-cytochrome b_5 reductase protein, and a terminal cyanide-sensitive desaturase protein.

The rejections over Ntambi (1996) of canceled Claims 1-4 are moot. The rejections over Ntambi of Claims 6 and 11 are traversed because Ntambi does not show the claimed methods to be operable in a human or non-human subject. All of the work presented in Ntambi was undertaken in cells *in vitro*. For that reason, it also follows that Ntambi did not, and could not, show increased insulin sensitivity in a human or non-human animal. Accordingly, for at least these two reasons, Ntambi fails to disclose every element of the rejected claims. The claimed ability to increase insulin sensitivity by reducing SCD1 activity was not known or shown until the inventors of the present application showed it in an $SCD^{-/-}$ knockout animal.

Rejections under 35 U.S.C. 103(a) for alleged obviousness

The rejections of canceled Claim 1 for alleged obviousness is moot. The rejections of Claims 7 and 11 are traversed because the combination of Crooke and Monia would not bring the skilled artisan to the invention. A skilled person reading Crooke's use of antisense to modulate SCD1 would not have found it obvious to recognize the effect of decreased SCD1 activity on insulin sensitivity, and Crooke would have had no basis for assuming any connection between the two. Indeed, the Examiner acknowledged that Crooke did not teach measuring insulin sensitivity.

In citing Monia, the Examiner has failed to appreciate that Monia affected translation of a gene in the insulin signaling pathway to get increased insulin sensitivity. While that result is not in and of itself surprising, it bears little relation to Applicants' interference with SCD1 activity. SCD1 is not believed to be involved in the insulin signaling pathway, but rather is believed to be a gene involved in insulin metabolism. For this reason, the Examiner's reliance on use of an antisense oligonucleotide complementary to a gene unrelated to SCD1 is misplaced. Moreover,

the Examiner has not drawn any link between the cited documents and the proteins said to be inhibited in Claim 11.

Rejections under 35 U.S.C. 102(e) for alleged anticipation

The Examiner has cited an application by Hayden et al. for its disclosure in Claim 48 of a method for treating insulin resistance by administering an inhibitor of SCD1 protein expression or activity. The Hayden claim is based upon work performed by Applicants, who are named as inventors on the Hayden application. Before Hayden's earliest disclosure of Claim 48, Applicants measured glucose tolerance in male and female heterozygous (+/-) and homozygous (-/-) SCD1 mice fasted for 4 hours. Animals were administered 2g/kg body weight of glucose by oral gavage. Plasma glucose was measured at 10 minute intervals for a total of 70 minutes using the glucose oxidase method. Glucose was cleared out of the blood circulation of the homozygous mice faster than in the heterozygous mice. This indicated that the homozygous SCD1 mice or SCD1 knockout mice have increased insulin sensitivity than the heterozygous mice.

Reconsideration is respectfully requested.

Fees

Please charge the fee for a Request for Continued Examination under 37 C.F.R. § 1.17(e) to Deposit Account No. 17-0055.

A petition for an extension of time for three months accompanies this response so the response will be deemed to have been timely filed. No other fee is believed due in connection with this response, but should any other fee be due in this or any subsequent response, please consider this to be a request to charge the fee to the same Deposit Account Number 17-0055.

Respectfully submitted,

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